

# What Lessons Have Intensivists Learned During the Evidence-Based Medicine Era?

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Evidence-based medicine, in existence for just over two decades, has resulted in monumental changes in critical care medicine. In the last 20 years, practice has shifted from a reliance on expert opinion to a critical appraisal of the available literature to answer focused clinic questions.<sup>1</sup> Systematic examination of what works and what does not, while valuing clinic experience and patient preferences, has been a surprising and thought-provoking journey that has resulted in dramatic improvements in the care of the critically ill patient. Many of the lessons learned during the evidence-based medicine era would have never been predicted two decades ago.

In this chapter, we describe five important lessons learned in intensive care during the evidence-based medicine era:

1. We need to look beyond single randomized clinic trials (RCTs).
2. It is the small things that make a difference.
3. Accountability is critically important.
4. We often need to do less to patients rather than more.
5. It is the multidisciplinary intensive care unit (ICU) team, not the individual provider, that is the most responsible for good clinic outcomes and high-quality critical care.

## LOOKING BEYOND SINGLE RANDOMIZED CONTROLLED TRIALS

By critically appraising the entire body of literature on specific interventions and clinic outcomes, we have learned many lessons about what is most important in the delivery of critical care. However, we have learned that we must wait before we immediately embrace the results of a single randomized clinic trial (RCT) with very impressive results and instead base our clinic practices on more comprehensive, cautious, and critical appraisals of all of the available literature.

The last two decades of critical care research are filled with stories of impressive findings from single-center RCTs that could not be replicated in larger multicenter RCTs. Unfortunately, in many cases, the initial positive single-center results have been embraced by early adopters, only

to have the results refuted by subsequent follow-up trials. The story of tight glycemic control in critical illness is illustrative. A single-center study of the management of hyperglycemia in a population consisting primarily of postcardiac surgical patients found that intensive glucose management with insulin infusion with a target blood glucose of 80 to 110 mg/dL dramatically reduced mortality when compared with a more lenient target blood glucose of 160 to 200 mg/dL.<sup>2</sup> The results of this single-center study were embraced by many intensivists and rapidly generalized to a wide variety of critically ill patients. The factors behind this rapid adoption by the field are multiple, including ease of implementation and cost. Unfortunately, a subsequent similar study of medical patients showed no significant benefit of an intensive insulin therapy protocol in the critically ill medical patient.<sup>3</sup> Ultimately, the most comprehensive multicenter trial of medical and surgical critically ill patients found significantly increased mortality in the group randomized to a tight glycemic control protocol, compared with targeting a blood glucose level of less than 180 mg/dL. This excess mortality was likely due to the much higher rates of severe hypoglycemia.<sup>4</sup>

In 2001, the era of early goal-directed therapy (EGDT) was introduced through the publication of a single-center, randomized controlled trial. EGDT was widely adopted, and multiple subsequent published trials, all prospective cohort series, confirmed its benefit.<sup>5</sup> More recently, two large RCTs<sup>6,7</sup> failed to demonstrate a survival benefit when protocolized resuscitation was compared with "usual care." It is possible that these results, at least in part, reflect the effect of the original EGDT trial; the widespread adoption of aggressive, early resuscitation; and the broad-based implementation of the Surviving Sepsis Campaign Guidelines and bundles.<sup>8</sup> If this continues to define usual care, then perhaps it is no longer necessary to mandate specific protocols for resuscitation because it appears that standard sepsis management has evolved to be consistent with published protocols.

The evidence for the use of hydrocortisone in the treatment of septic shock is an example of a sepsis treatment in which the initial promising study was embraced quite early,<sup>9</sup> only to be questioned by subsequent conflicting evidence.<sup>10</sup> We are still awaiting the final answer about the

utility of the administration of corticosteroids as an adjunctive therapy in septic shock.

Activated protein C is an example of how little we still currently know about the pathobiology of sepsis and the difficulty in developing targeted therapies. Activated protein C as an adjunct therapy for patients with sepsis initially was thought to be quite promising,<sup>11</sup> but it was abandoned after subsequent randomized controlled trials failed to duplicate the original results.<sup>12</sup>

## SMALL THINGS MAKE A BIG DIFFERENCE

The evidence-based era has taught us that small, often neglected or overlooked details of everyday bedside care can play a large role in determining whether our patients survive their ICU stay. Pneumonia that develops after the initiation of mechanic ventilation (ventilator-associated pneumonia [VAP]) is associated with high morbidity and mortality and significantly increased costs for critically ill patients. Several simple targeted interventions to address this problem have significantly reduced VAP rates. Simply keeping our intubated patients' heads elevated at least 30 degrees rather than leaving them supine (as was customary two decades ago) has resulted in major reductions in VAP.<sup>13,14</sup> In addition, a focus on better oral hygiene of mechanically ventilated patients via the administration of oral chlorhexidine has even further reduced the VAP rates.<sup>15-18</sup>

Another simple small intervention in the evidence-based era, the early mobilization of our critically ill patients, has also been found to significantly improve patient outcomes. We previously kept critically ill patients immobilized for weeks on end in the belief that this was necessary for their recovery. The result was very high rates of ICU-acquired weakness that required prolonged periods of rehabilitation in ICU survivors.<sup>19</sup> More recent studies have shown dramatic improvements in functional status and significantly decreased ICU length of stay (LOS) when critically ill patients are mobilized as soon and as much as possible.<sup>20,21</sup>

## ACCOUNTABILITY IS IMPORTANT

Another important lesson learned during the evidence-based era is the importance of tracking clinic behavior through performance measures. Published reports have demonstrated a significant gap between intensivists' perceptions of their ability to adhere to current evidence-based medicine and actual practice.<sup>22</sup> This dichotomy has been noted in adherence to low tidal volume strategies in acute respiratory distress syndrome and other common "best ICU practices." These findings have led to the development of checklists and performance metrics to foster clinician accountability that have provided tangible improvements in clinic care. Multifaceted interventions using checklists have dramatically reduced catheter-related blood stream infections<sup>23</sup> as well as complications from surgical procedures.<sup>24</sup>

In acute situations, checklists have also been shown to improve delivery of care.<sup>25</sup> Continuous measurement of individual performance in the evidence-based medicine era has allowed ongoing, real-time feedback to individual clinicians and groups of providers. Application of this

approach to sepsis care has resulted in significant improvement in adherence to evidence-based guidelines and in patient outcomes.<sup>26</sup>

## DO LESS, NOT MORE

The evidence-based era has also taught us that we often should do less, not more, to and for our critically ill patients. We have learned that interrupting sedation and awakening mechanically ventilated patients each day, and thus reducing the amount of medication administered, can significantly reduce ICU LOS.<sup>27,28</sup> When coupled with a daily weaning trial, daily awaking of ICU patients significantly reduced mortality.<sup>29</sup> We have also learned that decreasing the need for mechanic ventilation by first using noninvasive strategies in specific groups of patients with acute respiratory distress can improve outcome.<sup>30</sup> In addition, use of smaller tidal volumes in mechanically ventilated patients has been shown to be lifesaving.<sup>31</sup> We have also learned that reducing the amount of blood given to patients can significantly improve outcomes.<sup>32,33</sup>

## IT IS NOT JUST THE INTENSIVIST

Finally, we have learned that it is not the physician, but rather the entire health-care team, that is responsible for the delivery of high-quality care in the ICU. In a large observational cohort study based on the Acute Physiology and Chronic Health Evaluation IV (APACHE IV) model for predicting ICU LOS, investigators found that the key factors for predicting ICU LOS were structural and administrative. Specific APACHE IV variables of importance include reduced nurse-to-patient ratios, specific discharge policies, and the utilization of protocols. Structural and administrative factors were significantly different in high-performing ICUs with decreased LOS when adjusting for patient variables.<sup>34,35</sup>

In addition, the use of weaning protocols managed by respiratory therapists has resulted in significant reductions in the duration of mechanic ventilation relative to the subjective individualized assessment of an ICU clinician.<sup>36,37</sup> In addition, it was recently shown that staffing academic ICUs with intensivists overnight did not change clinic outcomes.<sup>38</sup> Finally, a recently published study found that empowering critical care nurses to intervene when they witnessed breaches in sterility was a key component in reducing catheter-related blood stream infections.<sup>23</sup> Taken together, these and other data strongly suggest that it is not solely the intensivist, but the entire critical care team, that is the key to high-quality care.

In summary, it seems that lessons offered by evidence-based medicine suggest that patience, keeping it simple, paying attention to detail, and working as a team are the key elements of good clinic care.

## Key Points

1. Look beyond single randomized controlled trials.
2. Small things make a big difference.
3. Accountability is important.
4. Do less, not more.
5. It is not just the intensivist.

## AUTHORS' RECOMMENDATION

- Single randomized controlled trials may be misleading, and the totality of evidence should be evaluated.
- Simple interventions such as head of bed elevation and early mobilization make a significant difference to outcomes.
- Measuring performance levels with checklists and audit improves outcomes. Accountability is important.
- Taking a conservative approach to interventions and therapies appears to confer patient benefit: "do less, not more."
- High-quality organized multidisciplinary intensive care improves outcomes: it is not just the intensivist.

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